IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/804,760	Confirmation No. 7688
Applicants	:	Meir S. Sacks et al.	
Filed	:	March 19, 2004	
Title	:	COMPOSITIONS FOR RAISING URIC ACID LEVELS AND METHODS OF USING THE SAME	
TC/A.U.	:	1614	
Examiner	:	Zohreh Vakili	
Docket No.	:	MSS 65055	
Customer No.	:	29694	

APPEAL BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

March 17, 2008

Sir:

Appellants hereby appeal the rejection of the captioned case set forth in the Office Action dated July 13, 2007.

REAL PARTY IN INTEREST

The real party in interest is MEIR S. SACKS, an inventor and the assignee of the captioned application.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences that are believed to directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

Claims 1 and 4-10 are pending in the application.

Claims 1 and 4-10 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 94/00132 to Peeters (Peeters '132) in view of GB 2 280 110 to Howard et al. (Howard et al. '110).

Claims 1 and 4-10 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peeters '132 in view of Howard et al. '110 and further in view of U.S. Patent No. 5,762,936 to Ronzio et al. (Ronzio et al. '936).

Claims 2 and 3 are canceled.

Claims 1 and 4-10 are appealed. A listing of the appealed claims is presented in the Appendix.

STATUS OF AMENDMENTS

There are no outstanding amendments.

SUMMARY OF CLAIMED SUBJECT MATTER

As recited in independent Claim 1, the present invention relates to a method of treating an Alzheimer's patient, the method comprising administering a daily dosage of from 100 mg to less than 1,000 mg of hypoxanthine, xanthine and/or inosine to the patient. *See* page 3, paragraph [00013]; page 13, paragraph [00049]. The daily dosage further comprises an antioxidant (dependent Claim 4) (*see* page 5; paragraph [00016]). The antioxidant may be selected from vitamin C, vitamin C derivatives and vitamin E (dependent Claim 5) (*see* page 5; paragraph [00016]). The antioxidant may comprise a polyphenol (dependent Claim 6) (*see* page 5; paragraph [00016]) or vitamin C and a polyphenol (dependent Claim 7) (*see* page 5; paragraph [00017]). The daily dosage may further comprise a maximum of 500 mg of the hypoxanthine, xanthine and/or inosine (dependent Claim 8) (*see* page 13, paragraph [00049]). In dependent Claim 9, the daily dosage comprises hypoxanthine and in dependent Claim 10, the daily dosage comprises inosine. *See* page 13, paragraph [00049].

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether Claims 1 and 4-10 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Peeters '132 in view of Howard et al. '110.

Whether Claims 1 and 4-10 are properly rejected under 35 U.S.C. § 103(a) as being unpatentable over Peeters '132 in view of Howard et al. '110 and further in view of Ronzio et al. '936.

ARGUMENT

Claims 1 and 4-10 are patentable over Peeters '132 in view of Howard et al. '110

Claims 1 and 4-10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peeters '132 in view of Howard et al. '110. According to the Examiner, Peeters '132 discloses the treatment of Alzheimer's disease with guanosine and precursors and/or derivatives thereof, including xanthosine, as well as guanine, inosine, xanthine, hypoxanthine, 5' inosinic acid, and mono-, di- and triphosphates of guanosine. The Examiner states that Peeters '132 discloses pharmaceutical compositions comprising each of the disclosed compounds. The Examiner acknowledges that Claim 1 recites that the composition contains a "daily dosage amount" of from 100 mg to less than 1,000 mg, but states that, properly construed at its broadest, the recitation "daily dosage amount" is merely a recitation of intended use, and the claims encompass any composition which can be administered at the claimed daily rate of administration.

Appellants respectfully traverse the Examiner's contention that the recited "daily dosage amount" is merely a recitation of intended use. The presently claimed invention is a method of treating an Alzheimer's patient, wherein the method comprises administering a daily dosage of from 100 mg to less than 1,000 mg of hypoxanthine, xanthine and/or inosine to the patient. Thus, Claim 1 does not merely recite a "daily dosage amount", but rather requires administering a specified amount of hypoxanthine, xanthine and/or inosine to an Alzheimer's patient on a daily basis.

The Examiner further states that Peeters '132 discloses that xanthosine should be administered at dosages of from 20 mg/kg/day to 150 mg/kg/day. According to the Examiner, assuming a 50 kg person, this dosage would result in an administration of compositions of 1 to 7.5 grams per day. The Examiner states that one of ordinary skill in the art would have recognized that a suitable method of administering 1 gram of xanthosine, or more, per day would have been by administering in 500 mg oral dosage forms. The Examiner takes official notice of the fact that the determination of suitable dosage regimen for the therapeutic methods in Peeters '132, including the use of 500 mg dosage forms, was clearly within the purview of the artisan of ordinary skill at the time of Appellants' invention. The Examiner further states that the claims are obvious absent some demonstration of an

unexpected result coming from the claimed use of dosage forms containing less than 1 gram, or no more than 500 mg of xanthosine.

Appellants respectfully submit that Peeters '132 does not raise a *prima facie* case of obviousness of the presently claimed invention because those skilled in the art, reading the relatively high levels of uric acid precursors required to be administered by Peeters '132, would not be led to treat an Alzheimer's patient with less than 1,000 mg of hypoxanthine, xanthine and/or inosine per day, as presently claimed. Peeters '132 teaches that significantly higher levels of uric acid precursors must be administered in order to be effective. Appellants' present invention teaches a daily dosage range of hypoxanthine, xanthine and/or inosine from 100 mg to less than 1,000 mg and that high daily doses may have negative effects, e.g., gout or kidney failure. Accordingly, Peeters '132 does not render Claim 1 *prima facie* obvious.

The Examiner acknowledges that Peeters '132 differs from the claimed invention in that the reference does not disclose the inclusion of the elected additional ingredient vitamin C in the disclosed compositions. The Examiner relies upon Howard et al. '110 as a teaching that vitamin C should be included in a regimen of treating Alzheimer's. According to the Examiner, one of ordinary skill in the art, reasonably expecting the vitamin C of Howard et al. '110 to be beneficial in Peeters' method of treating Alzheimer's, clearly would have been motivated to have included Howard et al.'s vitamin C in the therapeutic regime disclosed by Peeters '132. The Examiner notes that it is well know that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose.

Howard et al. '110 does not remedy the above-noted deficiencies of Peeters '132. Even if the teachings of Peeters '132 and Howard et al. '110 could properly be combined (which Appellants deny), such a combination would not render the present claims *prima facie* obvious because the prior art does not teach or suggest a method of treating an Alzheimer's patient by administering a daily dosage of less than 1,000 mg of hypoxanthine, xanthine and/or inosine, as recited in Claim 1. Accordingly, Claims 1 and 4-10 are patentable over Peeters '132 in view of Howard et al. '110.

Claims 1 and 4-10 are patentable over Peeters '132 in view of Howard et al. '110 and further in view of Ronzio et al. '936

Claims 1 and 4-10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peeters '132 in view of Howard et al. '110 and further in view of Ronzio et al. '936. The Examiner repeats the arguments *supra* related to Peeters' 132 and Howard et al. '110. According to the Examiner, Ronzio et al. '936 discloses an antioxidant composition extract that contains phenolics that are predominantly in the form of polyphenols, including flavonoids and phenolic acids. The Examiner states that the extract is highly effective in stabilizing linoleic acid and maintaining ascorbic acid (vitamin C) in a reduced state. The Examiner refers to Ronzio et al. '936 as disclosing that the reduction of superoxide was obtained by hypoxanthine-xanthine oxidase and NBT (the reaction mixture contained hypoxanthine: 0.5 mM) and with xanthine-xanthine oxidase and NBT (the reaction mixture contained xanthine: 0.5 mM). According to the Examiner, polyphenols from the lentil husk methanol-water extract (LHME) can work synergistically with the vitamin C as an antioxidant.

The Examiner asserts that the intended rate of administration does not and cannot change the product itself and despite Appellants' recitation in Claim 1 of "daily dosage", all that the claim requires is that the composition comprises the claim-designated amounts of the therapeutic ingredient. According to the Examiner, one of ordinary skill preparing orally administrable compositions according to Peeters '132 clearly would have been motivated to have prepared those compositions in dosage forms containing amounts of the ingredients which would have been suitable for oral administration. The Examiner states that such dosage forms clearly encompass the amounts of hypoxanthine, xanthine and/or inosine recited in Appellants' pending claims because the intended dosage regimen does not change the product itself, and because Peeters suggests preparing dosage forms containing the claimed amount of uric acid precursors.

Appellants respectfully traverse the Examiner's contention that Appellants' rate of administration does not and cannot change the product itself and despite the recitation of "daily dosage" in Claim 1, all that the claim requires is that the composition comprises the claim-designated amounts of therapeutic ingredient. As discussed *supra*, the presently claimed invention is a method of treating an Alzheimer's patient, wherein the method comprises administering a daily dosage of from 100 mg to less than 1,000 mg of hypoxanthine, xanthine and/or inosine to the patient. Claim 1 requires administering a specified amount of hypoxanthine, xanthine and/or

inosine to an Alzheimer's patient on a daily basis. Further, as discussed *supra*, Peeters '132 does not suggest preparing dosage forms containing Appellants' claimed amount of uric acid precursors. Rather, Peeters '132 teaches that significantly higher levels of uric acid precursors must be administered in order to be effective. Thus, the dosage forms of Peeters '132 do not encompass the amounts of hypoxanthine, xanthine and/or inosine recited in Appellants' claims as the Examiner suggests.

The Examiner states that a skilled artisan is provided with ample instruction and motivation to use the teachings of Ronzio et al. '936 along with the teachings of Peeters '132. According to the Examiner, Ronzio et al. '936 teaches a mixture rich in polyphenols and vitamin C as beneficial in treating neurogenerative diseases (e.g., Alzheimer's). According to the Examiner, the artisan of ordinary skill reasonably expecting the vitamin C and polyphenols of Ronzio et al. '936 to be beneficial in Peeters '132 method of treating Alzheimer's would have been motivated to have included vitamin C as taught by Howard et al. 110 and polyphenols and vitamin C as taught by Ronzio et al. '936 in the therapeutic regimen disclosed by Peeters '132. Thus, the Examiner states that the claimed invention was *prima facie* obvious.

As discussed *supra*, Peeters '132 teaches that significantly higher levels of uric acid precursors must be administered in order to be effective. The determination of a dosage of the active ingredient is not within the level of one having ordinary skill in the art because those skilled in the art, reading the relatively high levels of uric acid precursors required to be administered by Peeters '132, would not be led to treat an Alzheimer's patient with less than 1,000 mg of hypoxanthine, xanthine and/or inosine per day, as presently claimed. Howard et al. '110 does not remedy the deficiencies of Peeters '132, and Ronzio et al. '936 also fails to remedy the deficiencies of Peeters '132. Even if the teachings of Peeters '132 and Howard et al. '110 and Ronzio et al. '936 could properly be combined, such a combination would not render the present claims *prima facie* obvious because the prior art does not teach or suggest a method of treating an Alzheimer's patient by administering a daily dosage of less than 1,000 mg of hypoxanthine, xanthine and/or inosine, as recited in Claim 1.

The Examiner points out that the addition of Ronzio et al. '936 is used to modify the Examiner's original rejection because Ronzio et al. '936 teaches the use of polyphenols and vitamin C along with hypoxanthine and xanthine as beneficial for treating neurodegenerative diseases. According to the Examiner, not only is the dosage amount being taught by Peeters

'132, Ronzio et al. '936 also teaches the incorporation of 0.50 mM of hypoxanthine or 0.5 mM of xanthine. The Examiner states that the determination of a dosage of the active ingredient is well within the level of one having ordinary skill on the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of a drug while minimizing adverse side effects. Therefore, the Examiner states that the optimum dosage would have been obvious to the skilled artisan with the teachings of Peeters '132 and Ronzio et al. '936.

Appellants respectfully traverse this rejection and the Examiner's contention that Ronzio et al. '936 teaches the use of polyphenols and vitamin C along with hypoxanthine and xanthine to treat neurodegenerative diseases. According to Ronzio et al. '936, an extract may be obtained from lentil seed coatings characterized by a certain phenolic content. These phenolics are predominantly in the form of polyphenols which possess a broad range of antioxidant activities against free radicals, including superoxides (i.e., to quench the superoxide). Importantly, the ability of the antioxidant obtained from the extract to reduce superoxide is determined by following the reduction of nitro blue tetrazolium (NBT) by superoxide. *See.* Col. 6, lines 6-8. In Ronzio's Example III, the reduction of superoxide was determined by following the reduction of NBT by superoxide generated by three systems of which system (i) was a mixture of hypoxanthine-xanthine oxidase and NBT and system (ii) was a mixture of xanthine-xanthine oxidase and NBT. These systems were used to generate superoxides in order to measure the effectiveness of the antioxidant obtained from the extract in quenching the superoxide radicals.

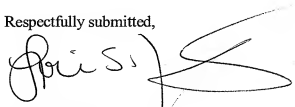
Example III of Ronzio et al. '936 is merely a classic mechanism for generating superoxides. This Example serves only to demonstrate the effective quenching of these superoxide radicals by the antioxidants (e.g., polyphenols) extracted from lentil seed coatings. It does not teach or suggest incorporation of 0.5 mM of hypoxanthine or 0.5 mM of xanthine with the polyphenols and vitamin C to treat neurodegenerative diseases as the Examiner suggests. Thus, the optimum dosage would not have been obvious to the skilled artisan with the teachings of Peeters and Ronzio et al. '936.

Accordingly, Claims 1 and 4-10 are patentable over Peeters '132 in view of Howard et al. '110 and further in view of Ronzio et al. '936.

Conclusion

For all of the reasons given above, Appellants respectfully submit that the rejections of Claims 1 and 4-10 under 35 U.S.C. § 103(a) are improper and should be reversed. It is therefore respectfully requested that the case is in condition for Notice of Allowance and, as such, that the case be remanded to the Examiner for the appropriate action.

Respectfully submitted,



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CLAIMS APPENDIX

1. A method of treating an Alzheimer's patient, the method comprising administering a daily dosage of from 100 mg to less than 1,000 mg of hypoxanthine, xanthine and/or inosine to the patient.

4. The method of Claim 1, wherein the daily dosage further comprises an antioxidant.

5. The method of Claim 4, wherein said antioxidant is selected from vitamin C, vitamin C derivatives and vitamin E.

6. The method of Claim 4, wherein said antioxidant comprises a polyphenol.

7. The method of Claim 4, wherein said antioxidant comprises vitamin C and a polyphenol.

8. The method of Claim 1, wherein said daily dosage of hypoxanthine, xanthine and/or inosine comprises a maximum of 500 mg.

9. The method of Claim 1, wherein the daily dosage comprises hypoxanthine.

10. The method of Claim 1, wherein the daily dosage comprises inosine.

EVIDENCE APPENDIX

None

RELATED PROCEEDINGS APPENDIX

None